II. REMARKS

Claims 1 to 4, 7 to 14, 18 to 22, and 24 to 26 are pending.

Claim 7 has been amended to incorporate the language of previously pending claim 8, and claim 8 has been amended to refer more specifically to "head and neck cancer". The amendment to claim 7 is supported by the language of claims 7 and 8 as originally filed. The amendment to claim 8 is supported, for example, at page 8, lines 2-8, and page 20, lines 13-16. As such, the amendments do not add new matter.

The objection to the specification and corresponding rejection of claims 1 to 4, 7 to 14, 18 to 22, and 24 to 26 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed.

It is stated in the Office Action that it is unpredictable whether one skilled in the art could use the claimed methods because, while the specification discloses that the recited "neoplastic" or "mutant" nucleic acids (i.e., APC, DCC, NF1, NF2, RET, VHL and WT-1) may be detected in tumor margins and lymph nodes that do not exhibit morphological characteristics indicative of a neoplastic pathology, the specification only exemplifies such detection of a different mutated nucleic acid (i.e., p53) in patients afflicted with head and neck cancer. It is further stated that Applicant's disclosure that p53 can be detected in histologically normal tissues is supported by the Deguchi et al. reference, which allegedly describes p53 mutations detected in histologically normal lymph nodes from prostate cancer patients, and the Nees et al. reference, which describes detecting mutated p53 in tumor margin tissues from patients with head and neck cancer, and teaches that the finding of p53 mutations in histologically normal tissue adjacent to tumor indicates that mutation of p53 is likely an early event in head and neck carcinogenesis.

Applicant submits that a review of the Deguchi et al. reference, particularly at Table 1, and page 5353, which are cited in the present Office Action, does not reveal any disclosure of p53 mutations, or their detection histologically normal lymph nodes from prostate cancer patients. Instead, Deguchi et al. describe the detection of prostate specific antigen (PSA) in prostate cancer cells, but not in normal cells, and indicate that PSA could be detected in lymph node cells that appeared to be histologically normal, thus providing a means for early identification of metastasis (see, e.g., Abstract, and page 5353, left column, second paragraph).

Although the results of Deguchi et al. can be distinguished from the claimed subject matter in that the PSA identified by Deguchi et al. is not a mutant nucleic acid, it is submitted that the reference provides objective evidence that, as disclosed in the subject application, the presence of cancer cells other than head and neck cancer cells can be detected in tissue that appears to be histologically normal. More specifically, Deguchi et al. provide confirmatory evidence that, as disclosed in the subject application, a marker specific for a primary cancer (i.e., PSA, which is specific for prostate cancer) can be detected in lymph nodes that appear histologically normal, thus providing an indication of metastasis of the primary tumor.

Applicant further submits that the skilled artisan, viewing the subject application, reasonably would have known that the claimed methods could be practiced with respect to the presently recited mutant nucleic acids (i.e., APC, DCC, etc.) because it was well known at the time the subject application was filed that mutations of the recited genes, like p53 mutations, occur in a variety of metastatic cancers (see, e.g., Table 1, page 11). More specifically, Applicant's disclosure that mutant p53 nucleic acid present in metastatic tumor cells can be detected in tissues that appear histologically normal (e.g., tumor surgical margin and lymph nodes) provides the general teaching that tumor cells that metastasize from a primary tumor can be identified in otherwise normal appearing tissues by detecting the mutant target nucleic acid present in the primary tumor cells. Thus, based on this disclosure, as exemplified using p53

mutations, the skilled artisan would have known that metastatic tumor cells having mutations of the recited genes similarly could be detected in histologically normal tissue such as lymph nodes and tumor margins.

In summary, it is submitted that one skilled in the art, viewing the specification, which discloses that tumor cells expressing a mutant p53 gene can be detected in histologically normal tissues such as tumor surgical margins and lymph nodes, and having knowledge of the Deguchi et al. reference, which describes detecting metastatic prostate cancer cells expressing PSA in histologically normal lymph nodes, would have predicted that the disclosed methods similarly could be used to detect a mutant APC, DCC, NF1, NF2, RET, VHL, or WT-1 nucleic acid, if present, in histologically normal tissues of a subject having a primary tumor containing such a mutant nucleic acid and, therefore, would have known how to practice the claimed methods without undue experimentation. Accordingly, it is respectfully requested that the objection to the specification be withdrawn, and that the corresponding rejection of claims 1 to 4, 7 to 14, 18 to 22, and 24 to 26 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, be removed.

In view of the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact the undersigned if there are any questions relating to the subject application.

Enclosed is Check No. 563594 in the amount of $110.00 in payment of the one (1) month extension of time fee. The Commissioner is hereby authorized to charge any other fees that may be associated with this communication, or credit any overpayment, to Deposit Account No. 50-1355.

Respectfully submitted,

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